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EXAMINER

LUCAS, ZACHARIAH

ART UNIT

PAPER NUMBER

1648

DATE MAILED: 06/04/2002

10

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/577,601

Applicant(s)

LOOSMORE ET AL.

Examiner

Zachariah Lucas

Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 09 May 2002.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above claim(s) 9 and 14-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☒ The proposed drawing correction filed on 09 May 2002 is: a) ☒ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All   b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election of Group I in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Applicant's election without traverse of species (A) in Paper No. 9 is acknowledged.
3. Claims 9 (as it reads on embodiments other than the elected species- Hia), and 14-43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions or species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9. Cancellation of the withdrawn claims, and amendment of claims to the elected species is requested.
4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### ***Information Disclosure Statement***

5. The information disclosure statement filed July 26, 2001 fails, in part, to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because it lacks copies of several of the non-patent literature references. It has been placed in the application file, but the information referred to therein which has not be submitted has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this

Art Unit: 1648

information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1). The references of which copies were submitted with the IDS have been considered by the examiner. The references not in the file are those numbered 1, 6, 10, 14-17, and 19.

### *Drawings*

6. The corrected or substitute drawings were received on May 9, 2002. These proposed corrections are found acceptable. Corrected drawings are required in the response to this office action.

### *Double Patenting*

7. Claims 1-3 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7 and 11 of U.S. Patent No. 5,506,139. The claims of the application at issue describe an expression vector encoding for a non-proteolytic analog of Hin47, its leader sequence, and a promoter, wherein said analog is a mutation of the natural protein in which at least one of the following residues has been substituted or deleted: residues 91, 121, and 195-201. The patent claims do not describe the presence of either the leader sequence or the promoter. Although the conflicting claims are not identical, they are not patentably distinct from each other because the presence of the leader sequence and a promoter in the current application do not patentably distinguish from the vectors claimed in the patent. The promoter is taught in the patent. See, col. 11, lines 3-15. The presence or absence of the

Art Unit: 1648

leader sequence is not discussed in the patent, however, the sequence is present in the Hin47 sequence shown in Figure 3 (seq. id. 2) of the patent. Thus, the patent claims read on vector embodiments that include the leader sequence.

8. The above rejection is, in part, based on the specification of a previously issued patent, rather than the claims. In support of the use of this material, the examiner notes the following excerpt from MPEP section 804:

When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. This does not mean that one is precluded from all use of the patent disclosure.

The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. In *re Boylan*, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In *re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in *Vogel* recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According to the court, one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined."

Thus, the courts have held that it is permissible to use the specification in determining what is included in, and obvious from, the invention defined by the claim on which the rejection is based. This is true even where elements are drawn from the specification describing the claimed invention which are not elements in the claim itself.

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Art Unit: 1648

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

*Specification*

10. The disclosure is objected to because of the following informalities: the specification refers to patent application number 09/268,347. pp. 3, line 18; 12, line 12, p16, line 31. This application is now patented, patent number 6,335,182. References to this and other applications in the specification must be updated.

Appropriate correction is required.

*Claim Rejections - 35 USC § 112*

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1 and 5, and dependant claims 6, 9-11, and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an expression vector encoding a non-proteolytic analog created by the substitution or deletion of one or more of amino acid residues 91, 121, and 197, does not reasonably provide enablement for any non-proteolytic Hin47 analog. The specification teaches only that "such an analog *may* be a mutation of natural Hin47 protein in which at least one amino acid selected from the group consisting of amino acids 91, 121, and 195 to 201 of natural Hin47 has been deleted or replaced by another amino acid." App. pp. 4-5 (*italics added*). This clearly implies that other such analogs may be

Art Unit: 1648

used, and therefore exist. However, no further guidance is given as to what other mutations of Hin47 may be encompassed by the phrase "non-proteolytic analog." While those skilled in the art would be aware that substitution or deletion of one or more of amino acids 91, 121, or 197 would have created a non-proteolytic analog of Hin47 (see, U.S. patent 5,506,139, cols. 5-6), the applicant has not described the creation of other non-proteolytic analogs in a manner that enables claims covering other analogs than those with such substitutions. This is for two reasons- first no guidance is given for what other analogs may be created, and second, no evidence is given that all analogs would have the same utility as the described analogs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

13. Claims 1, 2, 5, 6, and 7 are rejected under 35 U.S.C. 112, first paragraph. The specification, while being enabling for a non-proteolytic Hin47 analog wherein the analog includes a substitution or deletion of at least one of the amino acid residues 91, 121, or 197, does not reasonably provide enablement for the analog with the substitution or deletion of amino acids 195, 196, or 198-201. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. This is because the applicant has not shown that the substitution or deletion of any of amino acids 195, 196, or 198-201 would create a non-proteolytic analog.

U.S. Patent Number 5,506,139, issued to Loosmore et al. (the '139 patent), states that the residues 195 to 201 form an active site of the Hin47 and related proteases. Col. 5, lines 55-61. The patent also states that there is a consensus sequence of these active sites, wherein the consensus sequence varies from the Hin47 sequence at several residues. Id. Related protease

Art Unit: 1648

sequences have variations in their sequences corresponding to residues 196, 200, and 201. This indicates that substitutions of these residues would probably not affect the protease activity of the protein. Due to this, and because only residue 197 is identified as a part of the "catalytic triad" or essential elements of the protease (patent '139, col. 6, lines 1-5), the applicants have not shown that substitution or deletion of any of residues 195-201, other than residue 197, would result in a non-proteolytic analog.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 4, 12, and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims include the language "a plasmid vector having the *identifying characteristics of* plasmid..." (italics added). This phrase is indefinite as it does not state what the identifying characteristics of the plasmids are. The characteristics could be structural, functional, or both, or could mean that it is the precise plasmid shown in that figure that is being claimed. As the scope of the claim cannot be reasonably determined from the language of the claim, the claims are indefinite, and do not satisfy the requirements of 35 U.S.C. 112, paragraph 2.

### ***Claim Rejections - 35 USC § 102***

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

Art Unit: 1648

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by the 1998 Infection and Immunology article “The Haemophilus Influenzae HtrA Protein Is a Protective Antigen ” (the 1998 article) by Loosmore et al. These claims describe expression vectors comprising nucleic acid sequences encoding for non-proteolytic analogs of the Hin47 protein from a strain of Haemophilus. Claims 2 and 3 further limit the vector to vectors in which the sequence has one or more specific mutations.

The 1998 article discloses recombinant vectors for the production of Hin47 analogs. P. 900, col. 1. Among the analogs disclosed were several non-proteolytic analogs. See, abstract indicating that 8 of 9 recombinant mutant proteins had no measurable proteolytic activity. These analogs comprised of mutated DNA clones of the wild-type Hin47 gene. See, abstract. Among the mutations that are disclosed are H91A, D121A, and S197A- residues 91, 121, and 197 (accounting for the specific mutations described by claims 2 and 3). P. 900. cols. 1-2.

In its description of how the mutated clones were inserted into plasmids, the article states that “the Thr at position 27 was assumed to represent the start of the mature protein,” indicating (with a figure in the article showing) that part of the 5’ leader sequence was part of the vector prior to its insertion into a plasmid. P. 900, col. 1; and p. 901, fig.1 (showing the full length proteins, that include leader sequences, derived from the DNA clones). The fact that the clones produced proteins that include leader sequences indicates that the clones encoded for them. The article therefore disclosed vectors (the clones) encoding for Hin47 analogs with leader sequences.

Art Unit: 1648

18. Claim 4 is rejected under 35 U.S.C. 102(b) as being anticipated by the 139 patent. Claim 4 describes a plasmid vector "having the identifying characteristics of plasmid JB-3120-2 as seen in Figure 1A." As the claim does not identify what the identifying characteristics of the plasmid are, the claim is being read as any vector that expresses a non-proteolytic Hin47 analog wherein the analog is a H91A substitution mutant (because the analog encoded by the shown plasmid is a H91A mutant).

The 139 patent claims "recombinant plasmid... comprising a plasmid vector into which has been inserted" a Hin47 analog in which a substitution or deletion of one of the following amino residues has been made: residues 91, 121, and 195-201. Patent claims 14 and 7. Included in the potential substitutions is a substitution of H91 with alanine. Patent claim 11. Thus, the patent has described a plasmid that produces a H91A, which performs the same function as the plasmid JB-3120-2 in the application. As the function of the plasmid is the identifying characteristic of the plasmid, claim 4 is anticipated by the 139 patent.

### *Claim Rejections - 35 USC § 103*

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

20. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over the 139 patent in light of U.S. Patent Number 6,361,969, issued to Galeotti (the Galeotti patent) and Recombinant DNA, 2d edition, by Watson et al. For the purposes of this rejection, claim 4 is being read as

Art Unit: 1648

reading on a plasmid vector that comprises a promoter and encodes for a non-proteolytic Hin47 analog and its leader sequence.

The teachings of the 139 patent are described above in paragraphs 5 (describing a non-proteolytic Hin47 analog vector with a promoter and Hin47 leader sequence) and 11 (plasmid incorporating such vectors). Recombinant DNA teaches that plasmids are practical both for gene cloning and expression. Pp. 73-74, and 113. In view of the teachings described above, it would have been obvious to one of ordinary skill in the art to have made a plasmid according to claim 4.

The motivation for doing so would have been to make a plasmid vector that allows for the production of a Hin47 analog protein that would be secreted out of the cell producing it. The Galeotti patent teaches that inclusion of a leader sequence often allows for the secretion of a recombinant protein out of the cell. Col. 19, lines 43-50. Such secretion would simplify the collection of the proteins by allowing purification from the cell media, rather than first having to lyse the cells then purify the proteins from the cellular proteins.

21. Claims 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bass et al, J. Bacteriology (Bass), 178:1154-61, in view of the 1998 article (above), and U.S. Patent number 5,474,914, issued to Richard Spaete (the Spaete patent). These claims describe an expression vector comprising DNA encoding a non-proteolytic analog of Hin47, an additional protein, and a regulatory element. Claim 6 further requires that the vector also encode a Hin47 leader sequence. Claims 7 and 8 further limit the vector to one in which the Hin47 analog is a substitution or deletion mutant of one of the residues 91, 121, or 195-201 of the natural Hin47 sequence.

Art Unit: 1648

Bass teaches that the HtrA family of serine proteases may be used as chaperones for denatured proteins or proteins just secreted- when they do not lyse them. P. 1157. Thus, Bass indicates that Hin47, as a member of the HtrA family would be useful as a chaperone protein. However, Bass does not teach a Non-proteolytic Hin47, or the co-expression of Hin47 (with or without a leader sequence) with another protein to facilitate the secretion of itself and the other protein. The teachings of the 1998 article are given above. The article further teaches the inclusion of a Hin47 gene into a plasmid for recombinant production. However, this article does not teach the combination of Hin47 with another protein. Together, the two references teach that Hin47, in its non-proteolytic form, may be used a chaperone protein to other proteins. As Hin47 is no longer lytic, there is no longer a concern as to whether or not the other protein will be degraded or protected.

The Spaete patent teaches the co-expression of two recombinant proteins, a chaperone and a second protein, from a vector such that the non-chaperone protein is secreted or otherwise protected from degradation while in the recombinant host cell. Col. 2, lines 56-61. The patent teaches that any protein may be produced by this method so long as there is a compatible escort protein. Col. 8, lines 56-57. Spaete also teaches that secretion of the proteins may be enabled by including the leader sequence in the vector encoding for the chaperone, the leader sequence generally being a signal peptide directing cell secretion of the protein. Spaete patent, col. 21, lines 44-54. The reference does not specifically teach the use of a Hin47 analog as a chaperone protein. However, one of ordinary skill in the art would have known from the to references above that Hin47 could be used in the disclosed vector. Therefore, the vector described by claim 5 is obvious in light of the prior art.

One of ordinary skill in the art would have been motivated to use hin47 because it was known as being a chaperone (Bass and the 1998 article) when it does not lyse the target protein. The 1998 article teaches that the protease function may be eliminated by mutation. Thus, it would have been obvious to one of ordinary skill in the art to use the Hin47 analog in order to avoid the uncertainty involved in using the active protease.

22. Claims 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bass, in view of the 1998 article, and the Spaete patent, and further in view of Barenkamp and St. Geme III, *Molecular Microbiology* 19:1215-23 (Barenkamp), and U.S. Patent Number 6,335,182 (the 182 patent). These claims describe an expression vector encoding a non-proteolytic Hin47 analog, a regulatory element, and an additional nucleic acid molecule encoding for another recombinant protein, wherein that recombinant protein is the *Haemophilus influenzae* Hia protein.

The teachings of Bass, the 1998 article, and the Spaete patent are described above. The 1998 article further teaches that the HtrA analog may be effectively used as immunogens to *Haemophilus influenzae* (pp. 902, col. 2). These references therefore show that it would have been obvious to one of ordinary skill in the art to make an expression vector encoding for a Hin47 non-proteolytic analog and another protein to be recombinantly expressed. See paragraph 21 above. However, the references do not teach that the other protein to be expressed is the *Haemophilus influenzae* Hia protein.

Barenkamp teaches that the Hia protein may also be used as a vaccine against *Haemophilus influenzae*, especially in combination with other antigens. Pp. 1220-21. Thus, it would have been obvious to one of ordinary skill in the art to combine the Hin47 analog and Hia to make a multiantigenic vaccine for *Haemophilus influenzae*. Knowing that the two proteins

Art Unit: 1648

could be used together, it would have been obvious to one of ordinary skill in the art to make an expression system that produces both antigens. Thus, based on the references above, it would therefore have been obvious to one of ordinary skill in the art to make an expression vector encoding both the Hin47 analog and Hia.

The 182 patent further describes that a N-terminal truncated for of the Hia protein may also be used as a vaccine antigen. Col. 2, lines 53-65, col. 3, lines 45-47. The patent also specifically discloses the use of the V38 truncated protein. Col.2. line 65. thus, it would have been obvious to one of ordinary skill in the art to use the truncated protein, and the disclosed nucleic acid, in the vector also comprising the Hin47 analog.

23. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bass, in view of the 1998 article, and the Spaete patent, and further in view of Barenkamp the 182 patent and Recombinant DNA. This claim describes a "plasmid with the identifying characteristics of plasmid DS-2342-2-2." This plasmid contains a vector encoding for a Hin47 analog and its leader sequence, a promoter, and a truncated Hia protein. As the claim does not identify what characteristics identify the plasmid, the claim is being read as meaning a plasmid with the identifying characteristic of allowing the expression of both A Hin47 analog and a truncated Hia protein.

The teachings of the references other than Recombinant DNA are described above. The 139 patent describes the inclusion of the vectors described therein into plasmids, and Recombinant DNA states that plasmids are practical for DNA cloning- and expression of the genes in the plasmids. 139 patent, Claim 14; and Rec. DNA, pp. 73-74, and 113. From these

Art Unit: 1648

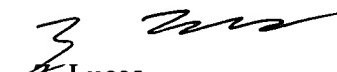
references, it would have been obvious to one skilled in the art to incorporate the vector encoding for the Hin47 analog and the truncated Hia protein into a plasmid.

*Conclusion*

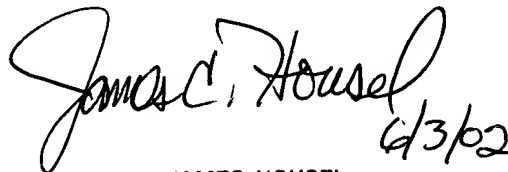
24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Z. Lucas  
Patent Examiner  
May 29, 2002



JAMES HOUSEL  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600